

WO 00/53114
PCT/GB00/00749

PATENT COOPERATION TREATY

PCT

NOTICE INFORMING THE APPLICANT OF THE
COMMUNICATION OF THE INTERNATIONAL
APPLICATION TO THE DESIGNATED OFFICES

(PCT Rule 47.1(c), first sentence)

From the INTERNATIONAL BUREAU

To:

DAVIES, Gregory, Mark
Urquhart-Dykes & Lord
Alexandra House
Alexandra Road
Swansea SA1 5ED
ROYAUME-UNI

COPY

Date of mailing (day/month/year) 14 September 2000 (14.09.00)		IMPORTANT NOTICE	
Applicant's or agent's file reference: P46619WO			
International application No. PCT/GB00/00749	International filing date (day/month/year) 03 March 2000 (03.03.00)	Priority date (day/month/year) 05 March 1999 (05.03.99)	
Applicant SLS BIOPHILE LIMITED et al			

1. Notice is hereby given that the International Bureau has communicated, as provided in Article 20, the international application to the following designated Offices on the date indicated above as the date of mailing of this Notice:
AU, KP, KR, US

In accordance with Rule 47.1(c), third sentence, those Offices will accept the present Notice as conclusive evidence that the communication of the international application has duly taken place on the date of mailing indicated above and no copy of the international application is required to be furnished by the applicant to the designated Office(s).

2. The following designated Offices have waived the requirement for such a communication at this time:

AE, AL, AM, AP, AT, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EA, EE, EP, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, OA, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW

The communication will be made to those Offices only upon their request. Furthermore, those Offices do not require the applicant to furnish a copy of the international application (Rule 49.1(a-bis)).

3. Enclosed with this Notice is a copy of the international application as published by the International Bureau on 14 September 2000 (14.09.00) under No. WO 00/53114

REMINDER REGARDING CHAPTER II (Article 31(2)(a) and Rule 54.2)

If the applicant wishes to postpone entry into the national phase until 30 months (or later in some Offices) from the priority date, a demand for international preliminary examination must be filed with the competent International Preliminary Examining Authority before the expiration of 19 months from the priority date.

It is the applicant's sole responsibility to monitor the 19-month time limit.

Note that only an applicant who is a national or resident of a PCT Contracting State which is bound by Chapter II has the right to file a demand for international preliminary examination.

REMINDER REGARDING ENTRY INTO THE NATIONAL PHASE (Article 22 or 39(1))

If the applicant wishes to proceed with the international application in the national phase, he must, within 20 months or 30 months, or later in some Offices, perform the acts referred to therein before each designated or elected Office.

For further important information on the time limits and acts to be performed for entering the national phase, see the Annex to Form PCT/IB/301 (Notification of Receipt of Record Copy) and Volume II of the PCT Applicant's Guide.

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. (41-22) 740.14.35	Authorized officer J. Zahra Telephone No. (41-22) 338.83.38
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PCT/GB00/00749

PATENT COOPERATION TREATY

PCT

NOTIFICATION CONCERNING
SUBMISSION OR TRANSMITTAL
OF PRIORITY DOCUMENT

(PCT Administrative Instructions, Section 411)

From the INTERNATIONAL BUREAU

To:

DAVIES, Gregory, Mark
Urquhart-Dykes & Lord
Alexandra House
Alexandra Road
Swansea SA1 5FD
ROYAUME-UNI

COPY

Date of mailing (day/month/year) 10 May 2000 (10.05.00)	IMPORTANT NOTIFICATION
Applicant's or agent's reference P46619W0	
International application No. PCT/GB00/00749	
International publication date (day/month/year) Not yet published	
Applicant SLS BIOPHILE LIMITED et al	International filing date (day/month/year) 03 March 2000 (03.03.00) Priority date (day/month/year) 05 March 1999 (05.03.99)

1. The applicant is hereby notified of the date of receipt (except where the letters "NR" appear in the right hand column) by the International Bureau of the priority document(s) relating to the earlier application(s) indicated below. Unless otherwise indicated by an asterisk appearing next to a date of receipt, or by the letters "NR", in the right-hand column, the priority document concerned was submitted or transmitted to the International Bureau in compliance with Rule 17.1(a) or (b).
2. This updates and replaces any previously issued notification concerning submission or transmittal of priority documents.
3. An asterisk (*) appearing next to a date of receipt, in the right-hand column, denotes a priority document submitted or transmitted to the International Bureau but not in compliance with Rule 17.1(a) or (b). In such a case, the attention of the applicant is directed to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.
4. The letters "NR" appearing in the right-hand column denote a priority document which was not received by the International Bureau or which the applicant did not request the receiving Office to prepare and transmit to the International Bureau, as provided by Rule 17.1(a) or (b), respectively. In such a case, the attention of the applicant is directed to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.

<u>Priority date</u>	<u>Priority application No.</u>	<u>Country or regional Office or PCT receiving Office</u>	<u>Date of receipt of priority document</u>
05 Marc 1999 (05.03.99)	9905173.2	GB	04 May 2000 (04.05.00)

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No. (41-22) 740.14.35

Authorized officer

Taïeb Akremi

Telephone No. (41-22) 338.83.38

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PCT INTERNATIONAL COOPERATION TREATY

PCT

NOTIFICATION OF THE RECORDING
OF A CHANGE(PCT Rule 92bis.1 and
Administrative Instructions, Section 422)

From the INTERNATIONAL BUREAU

To:

DAVIES, Gregory, Mark
Urquhart-Dykes & Lord
Alexandra House
Alexandra Road
Swansea SA1 5ED
ROYAUME-UNI

Date of mailing (day/month/year) 28 November 2000 (28.11.00)	IMPORTANT NOTIFICATION
Applicant's or agent's file reference P46619WO	
International application No. PCT/GB00/00749	International filing date (day/month/year) 03 March 2000 (03.03.00)

1. The following indications appeared on record concerning:



the applicant



the inventor



the agent



the common representative

Name and Address

KIERNAN, Michael, Noel
89 Heol Heddwch
Seven Sisters SA10 9AW
United Kingdom

State of Nationality

GB

State of Residence

GB

Telephone No.

Facsimile No.

Teleprinter No.

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:



the person



the name



the address



the nationality



the residence

Name and Address

KIERNAN, Michael, Noel
11 Roman Court
Blackpill
Swansea SA3 5BL
United Kingdom

State of Nationality

GB

State of Residence

GB

Telephone No.

Facsimile No.

Teleprinter No.

3. Further observations, if necessary:

4. A copy of this notification has been sent to:



the receiving Office



the designated Offices concerned



the International Searching Authority



the elected Offices concerned



the International Preliminary Examining Authority



other:

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

Christine Carrié

Telephone No.: (41-22) 338.83.38

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PATENT COOPERATION TREATY

PCT

NOTIFICATION OF THE RECORDING
OF A CHANGE(PCT Rule 92bis.1 and
Administrative Instructions, Section 422)

From the INTERNATIONAL BUREAU

To:

DAVIES, Gregory, Mark
Urquhart-Dykes & Lord
Alexandra House
Alexandra Road
Swansea SA1 5ED
ROYAUME-UNI

Date of mailing (day/month/year) 28 November 2000 (28.11.00)	IMPORTANT NOTIFICATION
Applicant's or agent's file reference P46619WO	
International application No. PCT/GB00/00749	International filing date (day/month/year) 03 March 2000 (03.03.00)

1. The following indications appeared on record concerning:

☒ the applicant

 ☐ the inventor

 ☐ the agent

 ☐ the common representative

Name and Address

SLS BIOPHILE LIMITED
Units 1 & 2 Heol Rhosyn
Dafen Industrial Estate
Llanelli
Carmarthenshire SA14 8LX
United Kingdom

State of Nationality

GB

State of Residence

GB

Telephone No.

Facsimile No.

Teleprinter No.

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

☒ the person

 ☒ the name

 ☒ the address

 ☐ the nationality

 ☐ the residence

Name and Address

ICN PHOTONICS LIMITED
Units 1 & 2 Heol Rhosyn
Parc Dafen Industrial Estate
Llanelli
Carmarthenshire SA14 8QG
United Kingdom

State of Nationality

GB

State of Residence

GB

Telephone No.

Facsimile No.

Teleprinter No.

3. Further observations, if necessary:

4. A copy of this notification has been sent to:

<input checked="" type="checkbox"/> the receiving Office	<input type="checkbox"/> the designated Offices concerned
<input type="checkbox"/> the International Searching Authority	<input checked="" type="checkbox"/> the elected Offices concerned
<input checked="" type="checkbox"/> the International Preliminary Examining Authority	<input type="checkbox"/> other:

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

Christine Carrié

Telephone No.: (41-22) 338.83.38

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PATENT COOPERATION TREATY

PCT

NOTIFICATION OF THE RECORDING
OF A CHANGE(PCT Rule 92bis.1 and
Administrative Instructions, Section 422)

From the INTERNATIONAL BUREAU

To:

DAVIES, Gregory, Mark
Urquhart-Dykes & Lord
Alexandra House
Alexandra Road
Swansea SA1 5ED
ROYAUME-UNI

Date of mailing (day/month/year) 28 November 2000 (28.11.00)	IMPORTANT NOTIFICATION
Applicant's or agent's file reference P46619WO	
International application No. PCT/GB00/00749	International filing date (day/month/year) 03 March 2000 (03.03.00)

1. The following indications appeared on record concerning:

☒ the applicant ☒ the inventor ☐ the agent ☐ the common representative

Name and Address KIERNAN, Michael, Noel 89 Heol Heddwch Seven Sisters SA10 9AW United Kingdom	State of Nationality GB	State of Residence GB
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

☐ the person ☐ the name ☒ the address ☐ the nationality ☐ the residence

Name and Address KIERNAN, Michael, Noel 11 Roman Court Blackpill Swansea SA3 5BL United Kingdom	State of Nationality GB	State of Residence GB
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	

3. Further observations, if necessary:

4. A copy of this notification has been sent to:

<input checked="" type="checkbox"/> the receiving Office	<input type="checkbox"/> the designated Offices concerned
<input type="checkbox"/> the International Searching Authority	<input checked="" type="checkbox"/> the elected Offices concerned
<input checked="" type="checkbox"/> the International Preliminary Examining Authority	<input type="checkbox"/> other:

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer Christine Carrié Telephone No.: (41-22) 338.83.38
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PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Assistant Commissioner for Patents
United States Patent and Trademark
Office
Box PCT
Washington, D.C.20231
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year)
24 October 2000 (24.10.00)

International application No.
PCT/GB00/00749

International filing date (day/month/year)
03 March 2000 (03.03.00)

Applicant's or agent's file reference
P46619WO

Priority date (day/month/year)
05 March 1999 (05.03.99)

Applicant
KIERNAN, Michael, Noel et al

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:
05 October 2000 (05.10.00)

☐ in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was
☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Form PCT/IB/331 (July 1992)

Authorized officer

Juan Cruz

Telephone No.: (41-22) 338.83.38

GB0000749

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PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference P46619W0	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/GB 00/ 00749	International filing date (day/month/year) 03/03/2000	(Earliest) Priority Date (day/month/year) 05/03/1999
Applicant SLS BIOPHILE LIMITED et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 6 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☒ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☐ the text is approved as submitted by the applicant.

☒ the text has been established by this Authority to read as follows:

SKIN WRINKLE REDUCTION USING PULSED LIGHT

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☒ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

4
☐ None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No.

PCT/GB 00/00749

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61B18/20

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHEDMinimum documentation searched (classification system followed by classification symbols)
IPC 7 A61B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	CA 2 198 826 A (DUDLEY DENIS K) 28 August 1998 (1998-08-28) page 1, line 11 - line 29 page 2, line 9 - line 24 page 3, line 10 - page 4, line 2 page 5, line 14; tables 1-7	1-5, 7-14, 17-19
Y	---	15, 16
Y	EP 0 763 371 A (ESC MEDICAL SYSTEMS LTD) 19 March 1997 (1997-03-19) column 5, line 48 - column 6, line 48	15, 16
X	US 5 312 395 A (TAN OON T ET AL) 17 May 1994 (1994-05-17) column 1, line 66 - column 2, line 19 column 2, line 55 - column 3, line 7 --- -/--	1-13, 17-19



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

G document member of the same patent family

Date of the actual completion of the international search

23 June 2000

Date of mailing of the international search report

29/06/2000

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Petter, E

INTERNATIONAL SEARCH REPORT

International Application No.

PCT/GB 00/00749

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 97 28752 A (CLEMENT ROBERT MARC ;GEORGE DAVID SIMON (GB); JONES GARY LEWIS (GB) 14 August 1997 (1997-08-14) page 11, line 6 - line 22; claim 1 ---	1-5, 7-12, 17-19
A	WO 98 08568 A (CLEMENT ROBERT MARC ;KIERNAN MICHAEL NOEL (GB); SLS BIOPHILE LIMIT) 5 March 1998 (1998-03-05) the whole document -----	1

INTERNATIONAL SEARCH REPORT

International application No.
PCT/GB 00/00749

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 20-31
because they relate to subject matter not required to be searched by this Authority, namely:
Rule 39.1(iv) PCT - Method for treatment of the human or animal body by surgery
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB 00/00749

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
CA 2198826	A	28-08-1998	NONE		
EP 0763371	A	19-03-1997	US	5964749 A	12-10-1999
			AU	6431096 A	20-03-1997
			CA	2185196 A	16-03-1997
			JP	9103507 A	22-04-1997
US 5312395	A	17-05-1994	AU	7463991 A	10-10-1991
			AU	7562591 A	10-10-1991
			DE	69103409 D	15-09-1994
			DE	69103409 T	23-03-1995
			EP	0519964 A	30-12-1992
			WO	9113652 A	19-09-1991
			WO	9113653 A	19-09-1991
WO 9728752	A	14-08-1997	AU	1613497 A	28-08-1997
WO 9808568	A	05-03-1998	US	5983900 A	16-11-1999
			AU	3951197 A	19-03-1998
			EP	0932431 A	04-08-1999

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PCT

REC'D 05 APR 2001

WIPO PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference P46619WO	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/GB00/00749	International filing date (day/month/year) 03/03/2000	Priority date (day/month/year) 05/03/1999
International Patent Classification (IPC) or national classification and IPC A61B18/20		
Applicant ICN PHOTONICS LIMITED et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.



2. This REPORT consists of a total of 8 sheets, including this cover sheet.

- ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☐ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☒ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand 05/10/2000	Date of completion of this report 02.04.2001
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Lohmann, S Telephone No. +49 89 2399 2328 

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB00/00749

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, pages:

1-15 as originally filed

Claims, No.:

1-31 as originally filed

Drawings, sheets:

1/3-3/3 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB00/00749

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 1-31.

because:

☒ the said international application, or the said claims Nos. 20-31 relate to the following subject matter which does not require an international preliminary examination (*specify*):
see separate sheet

☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 1-19 are so unclear that no meaningful opinion could be formed (*specify*):
see separate sheet

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the said claims Nos. 20-31.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:
see separate sheet

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**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/GB00/00749

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

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Re Item III

- 1 The method for reducing wrinkles comprising the step of selectively heating capillaries in order to permit transfer of inflammatory mediators through the capillary wall as defined in claims 20-31 is regarded to be a method for treatment of the human or animal body by surgery, since said transfer intervenes in the structure of an organism.

Furthermore, it is clear from the description (see page 10, lines 21-29) that at least a partial removal of the epidermis has to be performed prior to application of the aforementioned method, thereby introducing an **additional** surgical step.

Therefore, claims 20-31 have not been searched. Moreover, according to Article 34(4)(a)(i) PCT and Rule 67.1(iv) PCT, no international preliminary examination is required to be carried out on these claims.

- 2 Although claims 1 and 7 have been drafted as separate independent claims, they appear to relate effectively to the same subject-matter and to differ from each other only with regard to the definition of the subject-matter for which protection is sought and in respect of the terminology used for the features of that subject-matter. The aforementioned claims therefore lack conciseness and do consequently not meet the requirements of Article 6 PCT.

In order to overcome this objection, it would have appeared appropriate define the relevant subject-matter in terms of a **single independent device claim** followed by dependent claims covering features which are merely optional (Rule 6.4 PCT).

In this respect, the applicant's attention is also drawn to the requirement of **unity of the invention** (Rule 13 PCT).

- 3 As indicated above, the present plurality of independent claims renders the definition of **the invention** according to Article 33(1) PCT unclear, thereby precluding a meaningful assessment of the regulations of novelty and inventive step.

Nevertheless, it seems appropriate to submit the following observations:

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4 Reference is made to the following documents:

D1: CA 2 198 826 A (DUDLEY D K) 28 August 1998

D2: US 5 312 395 A (TAN O T) 17 May 1994

D3: WO 97 28752 A (CLEMENT R M) 14 August 1997

5 The apparatus of both claims 1 and 7 are not new under Article 33(2) PCT.

5.1 Document D1 is regarded as closest prior art to the subject-matter of both claims 1 and 7, and insofar as these claims can be understood (see Section VIII), this document discloses an apparatus showing the following features (the references in parentheses applying to this document):

- a radiation delivery system and a pulsation system (cf. page 11, lines 23-30)
- the radiation delivered is of a wavelength bandwidth of less than 15 nm (inherently disclosed, as explained below) in at least one of the ranges 570-600 nm and 750-850 nm (i.e. 585 nm in table 2 and 750 nm in table 7)
- pulse energy rise time is at or below 200 μ s (inherently disclosed, as explained below)
- the energy density per pulse is at or below to 5 J/cm² per pulse (i.e. 4 J/cm² delivered in four pulses, cf. table 2).

The feature with regard to the wavelength bandwidth does not confer any limitation to claim 7, since a bandwidth of less than 15 nm for pulsed dye laser systems is a common feature, which is well known in the art. Standard dyes show an emission bandwidth of a few 10 nm **without** any laser mirror or diffractive element for coupling the beam, like e.g. a grating. The use of at least one laser mirror and a second mirror or a diffractive element as **necessary elements** typically results in a bandwidth within a range of **not more than a few nm**.

Although the rise time is not explicitly mentioned, it is inherently disclosed, since rise times of longer than 50-200 μ s with a pulsed dye laser system emitting pulses of only 450 μ s duration are only possible, if **particular efforts** are made. Moreover, the **thermal relaxation time** of the tissue, upon which considerations about the rise time are based, is explicitly discussed in D1 (see page 3, line 10 - page 4, line 2 and page 6, lines 3-30).

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Consequently, the apparatus of claim 1 is not new in the sense of Article 33(2) PCT. It is indicated, that the subject-matter of claim 1 is also anticipated by documents D2 (cf. col. 2, lines 55-57 and col. 3, lines 1-7) and D3 (cf. page 11, lines 6-16).

- 5.2 Dependent claims 2-6 and 8-19 do not contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of novelty or inventive step, respectively, the reasons being as follows:
- 5.2.1 The subject-matter of claims 2-5 is anticipated by document D1 (see e.g. table 2 and the above explanation with regard to the rise time).
- 5.2.2 The subject-matter of claim 6 consists in the selection of a pulse duration from the range of pulse durations described in document D1. It is moreover taught by documents D2 and D3 (see the passages referred to above).
- 5.2.3 The features brought forward in dependent claims 8-19 are merely directed towards straightforward possibilities or slight constructional changes and specifications in the device of claims 1 or 7, respectively, which come within the scope of the customary practice followed by persons skilled in the art, especially as the advantages thus achieved can readily be foreseen.

Re Item VII

- 1 The independent claims are not in the two-part form in accordance with Rule 6.3(b) PCT, which in the present case would be appropriate, with those features known in combination from the prior art (document D1) being placed in the preamble (Rule 6.3(b)(i) PCT) and with the remaining features being included in the characterising part (Rule 6.3(b)(ii) PCT).
A new single independent apparatus claim (cf. Item III) should therefore have been redrafted accordingly.
- 2 Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in document D1 is not mentioned in the description, nor is this document identified therein.

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- 3 The features of the claims are not provided with reference signs placed in parentheses (Rule 6.2(b) PCT).

Re Item VIII

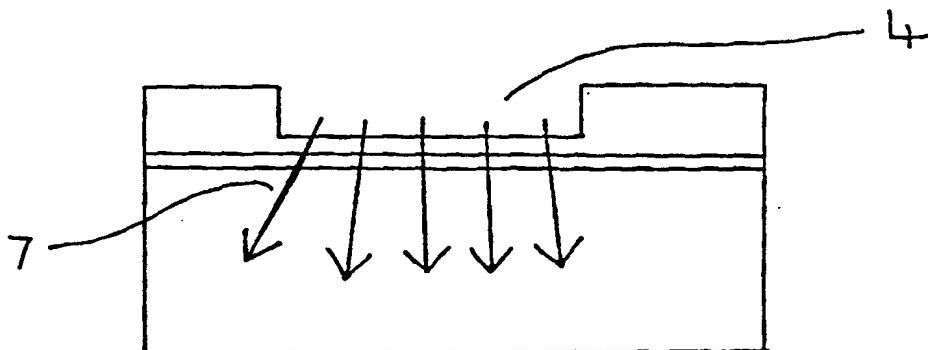
- 1 The expression "predetermined" does not confer any technical feature and consequently no limitation to independent claims 1 and 7 and dependent claim 13, thereby giving rise to an objection under Article 6 PCT.
It is furthermore not clear whether the term "regime" used in claims 1, 7 and 13 refers to a regime of wavelengths, pulse durations, rise times or energy densities; or even a combination of said parameters.
- 2 The relative term "**narrow** wavelength bandwidth" used in claims 1 and 16 has no well-recognised meaning and leaves the reader in doubt as to the meaning of the technical feature to which it refers, thereby rendering the definition of the subject-matter of said claims unclear in the sense of Article 6 PCT. Said term should have been specified according to the concrete (but nevertheless inherently disclosed, see Item III) value for the bandwidth of 15 nm, as set out in claims 7 and 8.
A similar objection holds for the terms "**concentrated** beam" and "**uniform** energy distribution", as brought forward in claims 9 and 10, respectively.
- 3 The expression "the apparatus being intended to be configured such that" used in claim 1 is vague and unclear and leaves the reader in doubt as to the meaning of the technical features to which it refers, thereby rendering the definition of the subject-matter of said claim unclear (Article 6 PCT).

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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁷: A61B 18/20	A1	(11) International Publication Number: WO 00/53114 (43) International Publication Date: 14 September 2000 (14.09.00)
(21) International Application Number: PCT/GB00/00749 (22) International Filing Date: 3 March 2000 (03.03.00) (30) Priority Data: 9905173.2 5 March 1999 (05.03.99) GB (71) Applicant (for all designated States except US): SLS BIO-PHILE LIMITED [GB/GB]; Units 1 & 2 Heol Rhosyn, Dafen Industrial Estate, Llanelli, Carmarthenshire SA14 8LX (GB). (72) Inventors; and (75) Inventors/Applicants (for US only): KIERNAN, Michael, Noel [GB/GB]; 89 Heol Heddwch, Seven Sisters SA10 9AW (GB). CLEMENT, Robert, Marc [GB/GB]; 11 Plas Road, Rhos, Pontardawe SA8 3HD (GB). (74) Agent: DAVIES, Gregory, Mark; Urquhart-Dykes & Lord, Alexandra House, Alexandra Road, Swansea SA1 5ED (GB).		(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i>
(54) Title: SKIN WRINKLE REDUCTION USING PULSED LIGHT		
(57) Abstract Wrinkles are cosmetically removed from a superficial area of mammalian skin tissue having an epidermal layer, a basal layer, and a dermal layer, by irradiating the dermal layer through the basal layer, the irradiation having an energy density in the range 5J/cm ² or less, and being selected to be absorbed by a chromophore in the dermal layer such that collagen present in the dermal layer is heated, while the basal layer remains intact so as to substantially inhibit contact of the dermal layer with ambient air.		



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INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 00/00749

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61B18/20

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	CA 2 198 826 A (DUDLEY DENIS K) 28 August 1998 (1998-08-28) page 1, line 11 - line 29 page 2, line 9 - line 24 page 3, line 10 -page 4, line 2 page 5, line 14; tables 1-7	1-5, 7-14, 17-19
Y	---	15, 16
Y	EP 0 763 371 A (ESC MEDICAL SYSTEMS LTD) 19 March 1997 (1997-03-19) column 5, line 48 -column 6, line 48 ---	15, 16
X	US 5 312 395 A (TAN OON T ET AL) 17 May 1994 (1994-05-17) column 1, line 66 -column 2, line 19 column 2, line 55 -column 3, line 7 --- -/-	1-13, 17-19

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

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X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

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8 document member of the same patent family

Date of the actual completion of the international search

23 June 2000

Date of mailing of the international search report

29/06/2000

Name and mailing address of the ISA

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INTERNATIONAL SEARCH REPORT

International Application No.

PCT/GB 00/00749

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 97 28752 A (CLEMENT ROBERT MARC ;GEORGE DAVID SIMON (GB); JONES GARY LEWIS (GB) 14 August 1997 (1997-08-14) page 11, line 6 - line 22; claim 1 ---	1-5, 7-12, 17-19
A	WO 98 08568 A (CLEMENT ROBERT MARC ;KIERNAN MICHAEL NOEL (GB); SLS BIOPHILE LIMIT) 5 March 1998 (1998-03-05) the whole document -----	1

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB 00/00749

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
CA 2198826	A	28-08-1998	NONE	
EP 0763371	A	19-03-1997	US 5964749 A	12-10-1999
			AU 6431096 A	20-03-1997
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			AU 3951197 A	19-03-1998
			EP 0932431 A	04-08-1999

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SKIN WRINKLE REDUCTION USING PULSED LIGHT

5 The present invention relates to a method of reducing wrinkles from a superficial area of mammalian skin tissue, and apparatus therefor.

10 The application of laser technology in healthcare is well known, and the use of lasers in medical applications has been studied extensively since the early 1960's. In recent years an increasing interest has been shown in cosmetic applications. Two such cosmetic applications are skin resurfacing and wrinkle removal; in this field lasers
15 can be used as an alternative to surgical facelifts.

20 There is a distinct difference between wrinkle removal and skin resurfacing. Skin resurfacing is where laser energy vaporizes thin layers of the epidermis without breaking through the basal layer into the dermis. This is essentially a superficial process primarily used to give the skin a "fresher" appearance. However, wrinkle removal as a more aggressive technique where tissue is removed layer by layer, invading the dermis and effectively
25 inducing a second degree burn. Heat is deposited in the dermis shrinking the collagen and tightening the skin.

30 In young skin, the collagen just beneath the surface of the skin forms an organized lattice with good elasticity and flexibility. During aging, the collagen changes its structure impacting negatively on the cosmetic appearance

of the skin. Several techniques have been developed to induce a "controlled injury" to the dermis in an attempt to generate rejuvenation of the collagen structure returning the skin to an earlier cosmetic appearance. During the 1990's a laser approach to wrinkle removal has been introduced.

For known wrinkle removal techniques, the wavelength is chosen so that the laser energy is highly absorbed in water, the current lasers of choice being the CO₂ laser at 10.6 μ m wavelength and the Erbium YAG laser at 2.94 μ m wavelength. In this non-selective process, pulses of laser energy are applied to the skin surface, each pulse vaporizing a layer of tissue between 30 μ m to 60 μ m in thickness. Normally, the first pass of the laser removes a thin layer of the epidermis without damaging the basal layer. Successive passes over the same area penetrate into the dermis and heat the collagen. The laser operator sees this thermal build-up "shrink" the skin in "real time", tightening up the skin's appearance. When the desired clinical outcome is achieved, the operator ceases applying laser pulses. It is therefore apparent that the quality of the cosmetic result is highly dependent upon the experience and skill of the operator.

In the case of CO₂ laser wrinkle removal, post-treatment supervision of the patient is a necessity. Immediately after treatment, the skin is essentially an open wound requiring dressings in place for 2-10 days. Additionally, topically applied lotions are required for patient comfort and prevention of infection. Post-operative infection is

common, primarily due to removal of the natural protective barrier of the skin, with a reported incidence of between 4.5 to 7%.

5 On average, with CO₂ laser wrinkle removal, post-treatment erythema is present for 4-5 months. This compares to 2-3 months following a Chemical Peel. Also, the incidence of side effects is significant, the most common being hyperpigmentation occurring in 30-40% of cases. Higher
10 incidences are reported in darker skin types. A delayed hypopigmentation, which can occur up to a year after the procedure was performed, has recently emerged as a complication of aggressive laser resurfacing. Many of the eminent laser resurfacing surgeons have resorted to less
15 aggressive techniques.

The effect of known procedures is two fold:

(a) the laser induces denaturing of the collagen in the
20 dermis, and the formation of cross links, which results in a tightening effect stretching the skin, reducing or removing the wrinkles (it is thought that the thermal threshold for this effect is a temperature of 70°C); and

25

(b) the changes to the dermis induce the generation of new collagen which develops using the matrix created by the denatured collagen as a foundation.

30

The skin-resurfacing and wrinkle removal procedure outlined above is considered by many experts in the field

as a significant improvement over previously used surgical methods. The procedure uses the laser's ability to deliver high energy density at the surface of tissue and hence ablate the surface tissue in a well controlled manner. Continuing to remove the tissue, layer by layer is designed to damage the collagen and hence induce wrinkle removal. This second stage of the procedure is primitive; the skin weeps, scabs form and redness of the skin appears for many weeks.

It is therefore the primary object of the present invention to provide a technique for removing wrinkles from a superficial area of mammalian skin tissue without causing secondary burns and other problems associated with traditional wrinkle removal.

The present invention provides a method of removing wrinkles from a superficial area of mammalian skin tissue. The dermal layer of the tissue is irradiated through the basal layer by radiation selected to be absorbed by a chromophore in the dermal layer such that collagen present in the dermal layer is heated, while the basal layer remains intact so as to substantially inhibit contact of the dermal layer with ambient air.

A particular advance of the present invention relies on the specific targeting of smaller capillaries, typically of a diameter in the 15-20 μ m range located in the upper dermis. These smaller capillaries have fenestrations which permit transfer of inflammatory mediators from the vessel through the vessel wall structure without causing

injury to the tissue or vessel. Selective targeting of these vessels and minimisation of interaction with other tissue components results in significant enhancement of the process.

5

According to an important feature of the present invention the wavelength of the stimulating electromagnetic radiation is selected to be substantially in the range 500nm-850nm (more preferably 500-600nm) and the stimulating electromagnetic radiation is pulsed to have a rise time substantially at or below 200 μ s (preferably substantially in the range 1 μ s to 150 μ s, more preferably substantially in the range 5 μ s to 150 μ s).

10

The wavelength range specifically targets the capillaries, the primary chromophore being oxyhaemoglobin.

15

The rapid rise time of the energy delivered in a pulse is important because, for vessels in the quoted size range, the thermal relaxation time is short (typically of the order of 100 μ s to 200 μ s). This signifies that heat is lost from the targeted vessels at a rapid rate; it is therefore important to ensure that energy is delivered rapidly enough to stimulate migration of the required inflammatory mediators, whilst compensating for the heat lost during the energy pulse. Typically an energy pulse rise time in the order of 50 μ s to 150 μ s, with a pulse duration up to 100ms (more preferably up to 2ms) is adequate although lower pulse durations in the range of up to 200 μ s may be sufficient and preferable.

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The radiation delivery system beneficially delivers a radiation beam of predetermined monochromatic wavelength or narrow wavelength bandwidth to the skin.

5 The total radiation energy density delivered to the skin is preferably substantially at or below $5\text{J}/\text{cm}^2$ per pulse (preferably substantially in the range $0.5\text{J}/\text{cm}^2$ to $5\text{J}/\text{cm}^2$ per pulse).

10 An artificial chromophore may be introduced into the desired area for wrinkle reduction, or a naturally occurring chromophore may be selected. In a preferred embodiment of the technique, the naturally occurring chromophore selected is oxyhemoglobin of the dermal plexus
15 which has wavelength absorption peaks at 585nm and 815nm, at which wavelengths absorption in surrounding tissue components is relatively low.

According to a further aspect, the invention therefore
20 provides apparatus for cosmetic reduction of wrinkles on a superficial area of mammalian skin, the apparatus comprising a radiation delivery system for delivering substantially monochromatic radiation in a bandwidth of substantially 15 nm or less in at least one of the ranges
25 570nm to 600nm and 750nm to 850nm, the delivery system including a pulsation system for pulsing the radiation delivered according to a predetermined regime in which the rise time of the energy pulse is substantially at or below $200\mu\text{s}$ (preferably substantially in the range $1\mu\text{s}$ to $150\mu\text{s}$,
30 more preferably substantially in the range $5\mu\text{s}$ to $150\mu\text{s}$).

The energy density of the substantially monochromatic radiation in the bandwidth of substantially 15nm or less delivered to the skin is preferably substantially at or below 5J/cm² per pulse.

5

10

The method according to the invention is non-invasive and non-ablative and can readily be performed by non-medical personnel. The total energy delivered per pulse is sufficient to effect the required physical change in the tissue surrounding the target chromophore without causing ablation of the target or other skin components through which the radiation passes.

5

The radiation is preferably substantially monochromatic or at least of a relatively narrow wavelength bandwidth to ensure that it is preferentially selectively absorbed by the target chromophore. A laser source may be used to produce the required wavelength, or a filtered broad band light source, such as an LED may be used with appropriate filtering to permit the selected wavelength (or narrow wavelength band) to pass.

The irradiation may be by means of a source of visible or infra-red radiation (suitably filtered to remove deleterious ultra-violet radiation if necessary). The radiation may be coherent (that is from a laser source). Such a laser source may be, for example, a dye laser, a ruby laser, or a semiconductor laser. If a dye laser is used, its wavelength is preferably such that it is absorbed by oxyhemoglobin (as naturally occurring chromophore present in blood vessels in the dermis).

Alternatively, the superficial area may be treated with an artificial chromophore which is absorbed into the dermal layer. Such an artificial chromophore may be applied to the epidermal layer in the form of a liposome-containing topical formulation. The chromophore may then permeate through the basal layer for delivery to the dermal layer.

When a laser is used, it may be arranged to scan the superficial area and/or to irradiate the dermal layer in pulses. When the laser is in pulsed mode, the pulses typically have duration of $10\mu\text{sec}$ to 10msec (more preferably $200\mu\text{sec}$ to 1msec).

It is sometimes desirable to remove part of the epidermis prior to irradiating the dermal layer according to the invention. Such epidermis removal (known as skin resurfacing) may be effected mechanically (for example by abrasion), or by means of laser radiation. When laser radiation is used for this purpose, it is typically a scanner controlled CO_2 laser source.

The energy density per pulse is preferably accurately controlled to ensure that a maximum threshold level (substantially of $5\text{J}/\text{cm}^2$) is not exceeded.

The invention will now be further described in specific embodiments, by way of example only and with reference to the accompanying drawings, in which:

Figure 1 is a schematic representation of the three outermost layers of mammalian skin tissue;

Figure 2 is a schematic representation of partial removal of the epidermis (skin resurfacing), which is an optional step according to the invention;

5 Figure 3 is a schematic illustration of the result of a prior art method of wrinkle removal, which is surgical because it involves full removal of the epidermis in a selected area and therefore exposure of the dermis and consequent second degree burning;

10 Figure 4 is a schematic illustration of the result of the method according to the invention, showing that the epidermis is partially intact and the basal layer fully intact;

5 Figure 5, is a schematic diagram of a first embodiment of wrinkle reduction apparatus according to the invention;

Figure 6 is a schematic diagram of an alternate embodiment of wrinkle reduction apparatus according to the invention;

Figure 7 is a schematic representation of an optical delivery system forming part of apparatus according to the invention; and,

Figure 8 is a graphical representation showing the intensity profile of the radiation delivered using apparatus according to the invention.

Referring to Figure 1, the basic skin structure of mammalian skin tissue comprises three layers, the outermost epidermis 1 which is adjacent to the basal layer 2 and then the dermis 3.

5

10

Referring to Figure 2, partial removal of an area 4 of epidermis 1 by means of CO₂ laser radiation is known as skin resurfacing. This stage represents the first step of a prior art method but is an optional step according to the invention. Both the basal layer 2 and the dermis 3 are unaffected by the laser radiation.

15

As shown in Figure 3, prior art method of wrinkle removal results in complete removal of an area 5 of epidermis 1 and basal layer 2 by repeated exposure to CO₂ laser radiation. Partial removal of the dermis 3 also occurs, as represented by 6, leaving the dermis exposed to air. This causes a second degree burn which is slow to heal and a risk of infection.

20

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As shown in Figure 4, the method of wrinkle removal according to the invention results in partial removal of the epidermis 1 (this is an optional step as described in Figure 2 above) and the basal layer 2 is left intact, such that the dermis 3 is not exposed to air. Laser radiation 7 is applied to the tissue and selectively absorbed by a chromophore in the dermis 3, heating the collagen and shrinking the skin hence removing the appearance of wrinkles.

30

In a preferred embodiment, the target chromophore selected

is oxyhemoglobin in the dermis 3 which has absorbtion peaks at approximately 585nm and 815nm. The apparatus shown in Figure 5 comprises a laser radiation delivery system 101 comprising a flashlamp excited pumped dye laser including a laser head 102, dye reservoir 103 and pump 104. A flowmeter 105 regulates dye flow to the laser cavity in the laser head 102 and a cooling system 106 cools the laser head 102 and dye reservoir 103. The system is controlled by a microprocessor controller 107 which operates voltage control of a pulse forming network 108 (including a capacitor and inductor network) which initiates a discharge pulse and consequently a pulsed beam laser output from laser head 102. Voltage control and feedback is provided between the microprocessor controller 107 and pulse forming network 108 via link 109. Temperature monitoring feedback is provided between the cooling system and the controller 107 via link 110.

The system parameters and laser head operates to output controlled pulses of laser radiation having wavelength in the range 577nm to 585nm and a pulse duration typically in the range 200 μ s to 1ms. In view of the need to selectively target small capillaries in the dermis, the energy pulse rise time is accurately controlled to be sufficiently rapid to produce the desired selective heating effect (as described earlier in the specification). The energy pulse rise time is substantially at or below 150ms. To produce the required wavelength an appropriate laser dye is selected (such as Rhodamine 575 or Pyromethene 590), the concentration of the dye solution is controlled.

Control of the pulse duration for the dye laser arrangement 101 is achieved by accurate control of the energy delivered to the exciting flashlamps in the laser head 102 by tailoring the capacitor and inductor values in the pulse forming network 108.

The energy is delivered to the skin surface via a fiberoptic tube 112 (see Figure 7) and a focussing optical lens arrangement 113 which is configured to focus a light spot onto the skin tissue surface so as to have a spot diameter within the range 1mm to 10mm, and an intensity distribution across the spot diameter that is substantially uniform (i.e. "a top hat" distribution), as shown in Figure 8 having the required rapid rise time at or below 150ms. Providing optics to ensure that the uniform energy distribution results in even heating of the tissue without the occurrence of "hot spots" which could result in tissue damage/ablation.

The radiation parameters are also selected to ensure that the total radiation energy density delivered per pulse falls substantially within the range $0.5\text{J}/\text{cm}^2$ to $5\text{J}/\text{cm}^2$. It is particularly important that the selected upper threshold value ($5\text{J}/\text{cm}^2$) is not exceeded significantly as delivery of a higher energy densities of radiation per pulse can result in unwanted effects on the skin (such as ablation and/or other damage).

For the dye laser system 101 of Figure 1, the energy density of the radiation delivered to the skin is controlled by adjustment of the flashlamp output energy

(which in turn controls the laser output energy). The laser output energy in conjunction with the spot site determines the energy density delivered. Accurate control is achieved by control of the dye circulation rate, the dye temperature and the flashlamp output energy. Dye circulation rate is important because repeated pulsing of the same volume of dye, without circulation, reduces the output energy of the laser head 102. Increasing or decreasing the dye temperature has an affect on the energy output of the laser head 102. The flashlamp output energy is controlled by varying the voltage with which the capacitors in the pulse forming network 108 are charged; feedback of the capacitor voltage via link 109 is therefore important.

The energy density required will vary within the specified range from person to person, depending upon skin colour.

Referring to Figure 6, there is shown an alternative embodiment of apparatus for performance of the invention in which an LED or semiconductor laser device 202 may be utilised to produce the output radiation 220. A user interface 213 enables input into a microprocessor controller 207 which is used to control a power supply unit 214 to ensure that the required current is supplied to the LED or semiconductor laser device 220. A temperature sensor 215 provides temperature feedback via a link 210. Output 216 from controller 207 sets the current supplied by the power supply unit 214 to the device 202; input 217 into the controller 207 provides current monitoring feedback. Control of the pulse

duration is achieved by pulsing the current supply from power supply unit 214 to the LED or semiconductor laser device 202.

5 High intensity LED devices are capable of producing wavelengths corresponding to the 585nm absorption peak of oxyhaemoglobin. The optical system (including lens 113) may include filters arranged to narrow the band of radiation passing from the LED to the target area of the
10 skin. Where lasers are used, the output may be monochromatic. Alternatively, or in the case where LED's are used, the radiation delivered may be "effectively" monochromatic, or of a relatively narrow band width (typically within a band width of 15nm or less).

15 Where a semiconductor laser device is used, the output may correspond to the second (higher) absorption peak (815nm) for oxyhaemoglobin.

20 Whilst the invention has been described in relation to delivery of effectively monochromatic radiation (or within specific narrow band widths) at one or other of the oxyhaemoglobin absorption peaks of 585nm and 815nm, it is clear that the beneficial effect of the invention can be
25 achieved to a certain degree by using wavelengths relatively close to, but either side, of the respective absorption peaks. Preferred wavelength ranges for operation are 570nm to 600nm and 750nm to 850nm for targeting oxyhaemoglobin.

Where an artificial chromophore is used, the wavelength (or narrow band of wavelengths) is selected to correspond to a characteristic absorption wavelength of the relevant chromophore. It remains important to ensure that the total energy delivered per pulse is below the threshold damage level (approximately $5\text{J}/\text{cm}^2$).

In the embodiments described, it is important to ensure that there is not excess energy (and therefore heat) build-up in the target, and therefore the inter pulse duration is selected at a level to avoid this situation occurring. It is preferred that the pulse repetition rate is substantially in the range 3Hz maximum or less.

Claims:

1. Apparatus for cosmetic reduction of wrinkles on a superficial area of mammalian skin, the apparatus comprising a radiation delivery system for delivering electromagnetic radiation of light wavelength to the skin, the radiation delivery system including a pulsation system for pulsing the radiation delivered according to a predetermined regime, the apparatus being intended to be configured such that the radiation delivered the skin is of predetermined monochromatic wavelength or narrow wavelength bandwidth substantially in the range 500nm-850nm and pulse energy rise time substantially at or below 200 μ s.
2. Apparatus according to claim 1, wherein the pulse energy rise time substantially in the range 50 μ s to 150 μ s.
3. Apparatus according to claim 1 or claim 2, wherein the radiation energy density delivered to the skin substantially at or below 5J/cm² per pulse.
4. Apparatus according to any preceding claim, wherein the energy pulse duration is substantially at or below 100ms.
5. Apparatus according to claim 4, wherein the energy pulse duration is substantially at or below 2ms.

6. Apparatus according to claim 5, wherein the energy pulse duration is substantially at or below 200 μ s.

5 7. Apparatus for cosmetic reduction of wrinkles on superficial mammalian skin, the apparatus comprising a radiation delivery system for delivering substantially monochromatic radiation, said radiation
10 being in a wavelength bandwidth of substantially 15nm or less and in at least one of the ranges 570nm to 600nm and 750nm to 850nm, the delivery system including a pulsation system for pulsing the radiation delivered according to a predetermined regime in which the radiation delivered to the skin
15 has an energy density substantially at or below to 5J/cm² per pulse.

8. Apparatus according to any preceding claim, wherein the radiation delivery system is set up to deliver
20 substantially monochromatic radiation in a bandwidth of substantially 15nm or less substantially in at least one of the ranges 577nm to 585nm and 800nm to 815nm.

25 9. Apparatus according to any preceding claim, wherein the radiation delivery system is set up to deliver radiation in a concentrated beam having a cross-section with a substantially uniform energy distribution across said beam cross section.

30 10. Apparatus according to any preceding claim, wherein

the radiation delivery system is set up to deliver radiation in a concentrated beam having a diameter substantially in the range 1mm to 10mm.

- 5 11. Apparatus according to any preceding claim, wherein the radiation delivery system comprises a laser radiation delivery system.
- 10 12. Apparatus according to claim 11, wherein the laser radiation delivery system comprises a dye laser radiation delivery system.
- 15 13. Apparatus according to claim 12, wherein the dye laser radiation delivery system comprises a flashlamp pumped dye laser including a pulse forming network arranged to pulse the laser according to the predetermined pulse regime.
- 20 14. Apparatus according to claim 11, wherein the laser radiation delivery system comprises a semiconductor laser radiation delivery system.
- 25 15. Apparatus according to any of claims 1 to 11, wherein the radiation delivery means includes a broad band radiation emitting device.
- 30 16. Apparatus according to claim 12, wherein the radiation delivery means includes at least one radiation filter arranged to filter radiation to permit the substantially monochromatic (or narrowed bandwidth) radiation to be delivered to the skin.

17. Apparatus according to any preceding claim, further comprising a control system arranged to permit the energy density to be varied within the range $0.5\text{J}/\text{cm}^2$ and $5\text{J}/\text{cm}^2$.

18. Apparatus according to claim 17, wherein the control means is arranged to inhibit selection of an energy density substantially above $5\text{J}/\text{cm}^2$.

19. Apparatus according to any preceding claim, which includes an optical arrangement for focussing the radiation beam.

20. A method of cosmetically reducing wrinkles from a superficial area of mammalian skin tissue having, in the order specified, an epidermal layer, a basal layer, and a dermal layer, which method comprises irradiating said dermal layer through said basal layer by means of visible or infra-red radiation, said irradiation being selected to be absorbed by a chromophore in targeted capillaries present in said dermal layer, the targeted capillaries having fenestrations permitting transfer of inflammatory mediators through the capillary wall upon selective heating to a threshold level, while said basal layer remains intact so as to substantially inhibit contact of said dermal layer with ambient air, said irradiation being pulsed and having:

i) an energy density of substantially $5\text{J}/\text{cm}^2$

20

or less; and/or,

ii) energy pulse rise time substantially at or below 200 μ s.

5

21. A method according to claim 20, wherein the irradiation is from a substantially monochromatic radiation source in a bandwidth of substantially 15nm or less.

10

22. A method according to claim 21, wherein said irradiation is from a coherent radiation source.

15

23. A method according to claim 22, wherein the source comprises a ruby laser arranged to target the dermis.

20

24. A method according to claim 22, wherein the source comprises a dye laser of wavelength selected to target oxyhemoglobin present in blood vessels in said dermal layer.

25

25. A method according to claim 22, wherein the source comprises a dye laser, a ruby laser, or a semiconductor laser which scans said area of mammalian skin tissue.

30

26. A method according to according to any of claims 20 to 25, wherein the pulse energy rise time substantially in the range 50 μ s to 150 μ s.

27. A method according to any of claims 20 to 26, wherein the energy pulse duration is substantially at or below 100ms.

5 28. A method according to claim 27, wherein the energy pulse duration is substantially at or below 2ms.

29. A method according to claim 28, wherein the energy pulse duration is substantially at or below 200 μ s.

10 30. A method according to claim 20, in which said superficial area of mammalian skin tissue is treated with an artificial chromophore which is absorbed into the dermal layer.

15 31. A method according to claim 30, wherein the artificial chromophore is applied to the epidermal layer in the form of a liposome-containing topical formulation.

FIGURE 1

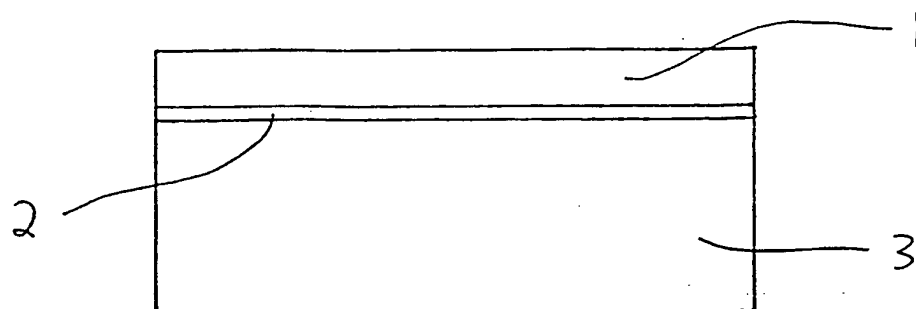


FIGURE 2

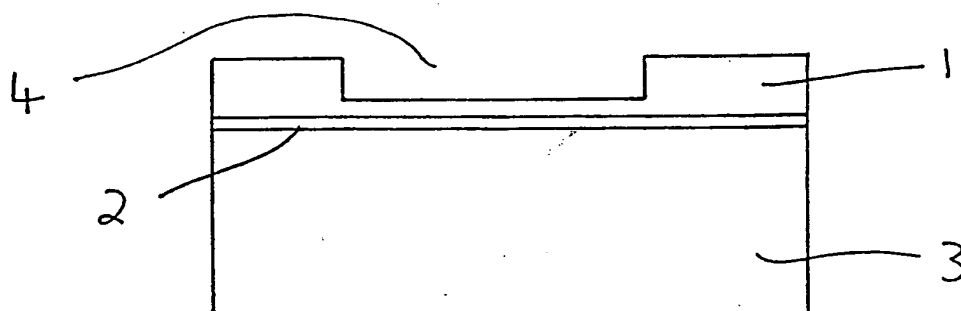


FIGURE 3

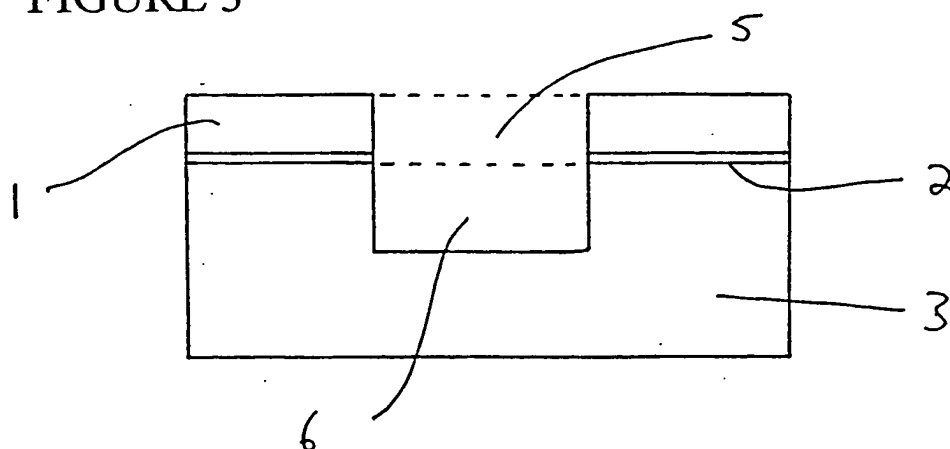


FIGURE 4

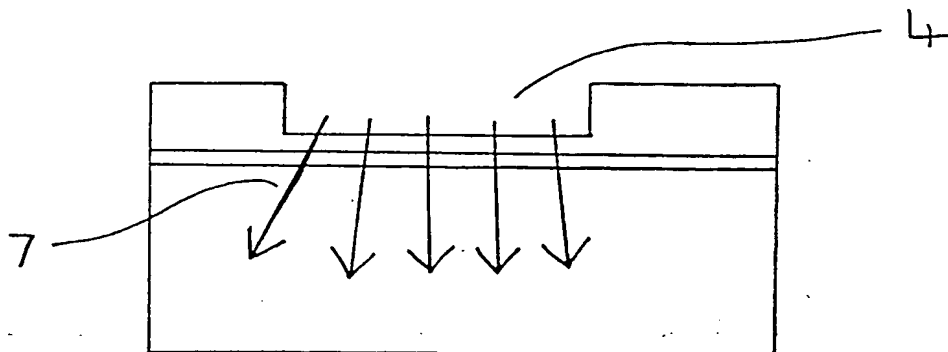


FIGURE 5

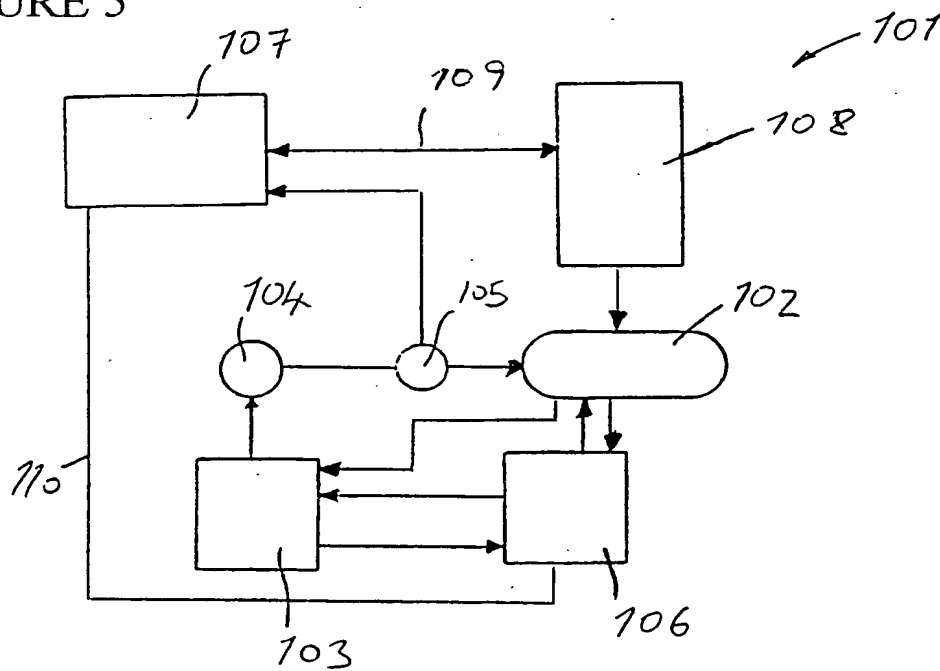


FIGURE 6

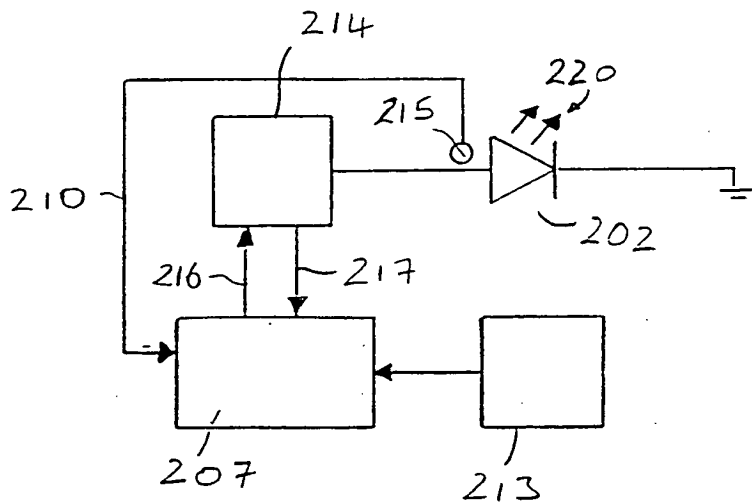


FIGURE 7

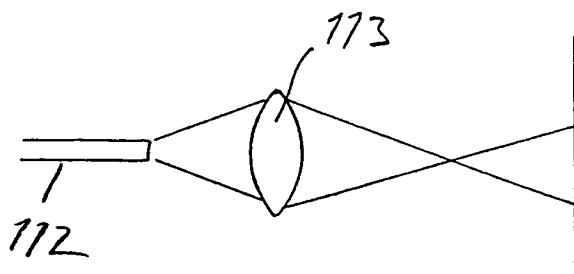
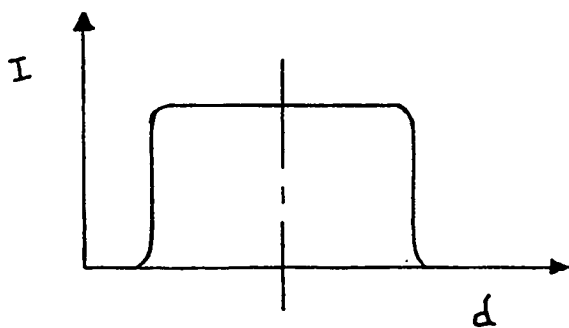


FIGURE 8



INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 00/00749

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61B18/20

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EP0-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	CA 2 198 826 A (DUDLEY DENIS K) 28 August 1998 (1998-08-28) page 1, line 11 - line 29 page 2, line 9 - line 24 page 3, line 10 - page 4, line 2 page 5, line 14; tables 1-7	1-5, 7-14, 17-19
Y	----	15, 16
Y	EP 0 763 371 A (ESC MEDICAL SYSTEMS LTD) 19 March 1997 (1997-03-19) column 5, line 48 - column 6, line 48	15, 16
X	US 5 312 395 A (TAN OON T ET AL) 17 May 1994 (1994-05-17) column 1, line 66 - column 2, line 19 column 2, line 55 - column 3, line 7 ----- -/--	1-13, 17-19

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

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Date of the actual completion of the international search

23 June 2000

Date of mailing of the international search report

29/06/2000

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INTERNATIONAL ARCH REPORT

International Application No

PCT/GB 00/00749

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

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